Multiparameter optimization for whole-brain model personalization

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Advancing therapies for neurological disorders relies on developing efficient, personalized whole-brain models that can capture mechanistic insights and pathological features. Current challenges in creating such computational models arise from managing a considerable number of adjustable parameters. The conventional manual exploration of this parameter space is a serious limitation for personalizing models to individual subject data [1].

This work aims to address this by approaching the problem as an optimization challenge in the context of developing brain models capable of characterizing individual pathology, particularly Alzheimer's disease (AD), with the ultimate goal of providing better transcranial electromagnetic stimulation protocols. For this purpose, we work with hybrid brain models [1] combining biophysical head models and a network of laminar neural mass models (LaNMM), each capable of representing slow (alpha) and fast (gamma) activity [2].

For the personalization of whole brain models, our approach takes into account two aspects. First, we include a parameter representing the global coupling strength, a parameter widely acknowledged in the literature [3], yet without explicit links to particular pathologies. Second, we optimize the Parvalbumin-positive cells (PV) to pyramidal synapse connectivity strength, tailored to model a suggested AD mechanism involving PV failure [4]. This modeling approach not only accounts for the pathology but also directs attention to gamma activity, a key biomarker of AD [5].

We navigated several steps for effective personalization: a dynamical landscape inspection, identifying parameter spaces reflecting realistic brain dynamics; the selection of an apt loss function, which can integrate fMRI functional connectivity; and finally, the exploration of methods tailored for non-convex landscapes, including Bayesian Optimization.

Finally, we present some initial results on a small set of personalized whole-brain models for both healthy and AD patients.

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